

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
ORION CORPORATION
ORION PHARMA
Legal Affairs and Intellectual
Property Rights, P.O. Box 65
Fin-02101 Espoo
FINLAND

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

<p>Date of mailing (day/month/year) 30/09/2004</p>	
<p>Applicant's or agent's file reference ATI - EPI</p>	<p>FOR FURTHER ACTION See paragraphs 1 and 4 below</p>
<p>International application No. PCT/FI2004/000220</p>	<p>International filing date (day/month/year) 08/04/2004</p>
<p>Applicant ORION CORPORATION</p>	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.
- Filing of amendments and statement under Article 19:**
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):
- When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.
- Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35
- For more detailed instructions,** see the notes on the accompanying sheet.
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, within **20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

<p>Name and mailing address of the International Searching Authority</p> <div style="display: flex; align-items: center;"> <div> <p>European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016</p> </div> </div>	<p>Authorized officer</p> <p style="font-size: 1.2em;">Joëlle Gerber</p>
--	--

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ATI - EPI	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/FI2004/000220	International filing date (day/month/year) 08/04/2004	(Earliest) Priority Date (day/month/year) 10/04/2003
Applicant ORION CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

USE OF AN ALPHA2-ADRENOCEPTOR ANTAGONIST FOR THE TREATMENT OF EPILEPSY

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/FI2004/000220

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 7 (all partially), 2

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1(partially),2,7(partially)

Use of an alpha2-adrenoceptor antagonist which is atipamezole for inhibiting the development of epilepsy

2. claims: 1(partially),3,6-7(partially)

Use of an alpha2-adrenoceptor antagonist which is idazoxan or an analog thereof for inhibiting the development of epilepsy

3. claims: 1(partially),4,6-7(partially)

Use of an alpha2-adrenoceptor antagonist which is efaroxan or an analog thereof for inhibiting the development of epilepsy

4. claims: 1(partially),5,6-7(partially)

Use of an alpha2-adrenoceptor antagonist which is an analog of atipamezole (e.g. 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole) for inhibiting the development of epilepsy

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/FI2004/000220

International filing date (day/month/year)
08.04.2004

Priority date (day/month/year)
10.04.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/00, A61K31/4164, A61K31/4178, A61P25/08

Applicant
ORION CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Hoff, P

Telephone No. +31 70 340-3520



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/FI2004/000220

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/FI2004/000220

Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/FI2004/000220

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1(partially), 3-6, 7(partially)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 1(partially), 3-6, 7(partially)
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/FI2004/000220

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1(partially),2,7(partially)

Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1,2,7
Inventive step (IS)	Yes: Claims	
	No: Claims	1,2,7
Industrial applicability (IA)	Yes: Claims	1,2,7
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/FI2004/000220

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)
and / or
2. Non-written disclosures (Rules 43*bis*.1 and 70.9)
see form 210

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/FI2004/000220

Re Item III.

In reply to the objection to lack of unity, the applicant has not paid additional search fees. The international search report has been established for the first invention only.

No opinion will be given in respect of subject-matter which is not covered by the search report (Rule 66.1(e) PCT).

Re Item IV.

The separate inventions/groups of inventions are:

1. Claims: 1(partially),2,7(partially)

Use of an alpha2-adrenoceptor antagonist which is atipamezole for inhibiting the development of epilepsy

2. Claims: 1(partially),3,6-7(partially)

Use of an alpha2-adrenoceptor antagonist which is idazoxan or an analog thereof for inhibiting the development of epilepsy

3. Claims: 1(partially),4,6-7(partially)

Use of an alpha2-adrenoceptor antagonist which is efaroxan or an analog thereof for inhibiting the development of epilepsy

4. Claims: 1(partially),5,6-7(partially)

Use of an alpha2-adrenoceptor antagonist which is an analog of atipamezole (e.g. 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole) for inhibiting the development of epilepsy

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The problem to be solved by the present invention is to provide a medicament for inhibiting the development of epilepsy in a patient at risk of developing epilepsy.

The proposed solution is to use an alpha2-adrenoceptor antagonist, in particular:

1a. atipamezole

- 1b. an analog of atipamezole (such as 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole)
2. idazoxan or an analog thereof
3. efaroxyan or an analog thereof

The alpha2-adrenoceptor antagonist property, represents the technical feature which may, a priori, unify the different compounds 1a, 1b, 2 and 3.

However, the use of alpha2-adrenoceptor antagonists for treating epilepsy has been already described in the state of the art.

XP8031700 describes the effect of atipamezole, a selective alpha2-adrenoceptor antagonist, on the recovery process from status epilepticus-induced brain trauma. Even if chronic treatment with atipamezole does not totally prevent epileptogenesis, there is, however, a clear disease-modifying effect; that is, the epilepsy that develops is milder and non-progressive.

XP8031693 discloses that atipamezole is able to reverse the proconvulsant action of dexmedetomidine.

EP-A-194984 and EP-A-304910 describe the use of various alpha2-adrenoceptor antagonists in the treatment of epilepsy.

Consequently, because alpha2-adrenoceptor antagonists, including atipamezole, have been already disclosed for treating epilepsy in the state of the art (see the various references mentioned above), the alpha2-adrenoceptor antagonist property can no longer serve as a single general inventive concept linking the different compounds 1) to 3) which have no other special technical features in common.

Moreover, since atipamezole has also been disclosed in relation to the inhibition of the development of epilepsy, there is no common inventive concept anymore between atipamezole and its analogs.

Therefore, the use of the compounds 1a, 1b, 2 and 3 for inhibiting the development of epilepsy represents each a distinct invention, characterised by its own special technical feature, i.e. the structural feature of the compounds.

In the present application no further technical feature(s) can be distinguished that can be regarded as a "special technical feature" involved in the technical relationship among the different inventions. Consequently, the present application lacks unity of

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/FI2004/000220

invention, and the different solutions not belonging to a common inventive concept are identified as the different subjects listed above. Each of the inventions listed is a distinct invention, characterised by its own special technical feature, defining the contribution which each of the claimed inventions, considered as a whole, makes over the prior art, i.e. the specific features of the individual compounds.

As the applicant has not had a search report drawn up on the other inventions, the present opinion will be established on the basis of the invention in respect of which a search has been carried out, in other words the first invention.

Re Item V.

1 The following documents are referred to in this communication:

- D1 : PITKANEN A (REPRINT) ET AL: "Disease modifying effects of alpha2-adrenoceptor blocker, atipamezole , on epileptogenesis in rats" EPILEPSIA, (FEB 2003) VOL. 44, SUPP. [8], PP. 175-175. PUBLISHER: BLACKWELL PUBLISHING INC, 350 MAIN ST, MALDEN, MA 02148 USA. ISSN: 0013-9580., February 2003 (2003-02), XP008031700
- D2 : MIRSKI MAREK A Z ET AL: "Dexmedetomidine decreases seizure threshold in a rat model of experimental generalized epilepsy" ANESTHESIOLOGY (HAGERSTOWN), vol. 81, no. 6, 1994, pages 1422-1428, XP008031693 ISSN: 0003-3022
- D3 : EP 0 194 984 A (CONTINENTAL PHARMA) 17 September 1986 (1986-09-17)
- D4 : EP 0 304 910 A (SEARLE & CO) 1 March 1989 (1989-03-01)

The Applicant's attention is drawn to the fact that the present opinion expressed as to novelty, inventive step and industrial applicability refers only to matter for which an international search report has been drawn up (i.e. the use of an alpha2-adrenoceptor antagonist which is atipamezole for inhibiting the development of epilepsy).

2 NOVELTY

- 2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1,2,7 is not new in the sense of Article 33(2) PCT. Document D1 discloses: the effect of atipamezole, a selective alpha2-adrenoceptor antagonist, on the recovery process from status epilepticus-induced brain trauma. Even if chronic treatment with atipamezole does not totally prevent epileptogenesis, there is, however, a clear disease-modifying effect; that is, the epilepsy that develops is milder and non-progressive.
- 2.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1,2,7 is not new in the sense of Article 33(2) PCT. Document D2 discloses: the ability of atipamezole to reverse the proconvulsant action of dexmedetomidine.
- 2.3 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1,7 is not new in the sense of Article 33(2) PCT. Documents D3 (page 1, lines 1-11; page 8, lines 4-21; page 58, lines 5-27; claim 28) and D4 (page 18, line 56-page 19, line 1) disclose: the use of various alpha2-adrenoceptor antagonists in the treatment of epilepsy.

3 INVENTIVE STEP

Should the Applicant have overcome the objections of lack of novelty raised above, an inventive step could not be acknowledged over D1, as the present subject-matter of claims 1,2,7, as far as novel, appears to be an obvious alternative over said documents (Article 33(3) PCT).

4 INDUSTRIAL APPLICABILITY

There are no doubts about industrial applicability (Art.33(4) PCT)